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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,188	09/14/2006	Diana Alonso Gordillo	18043-004US1 F/USP290109	3277

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EXAMINER	
CHANDRAKUMAR, NIZAL S	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
08/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,188	GORDILLO ET AL.	
	Examiner	Art Unit	
	NIZAL S. CHANDRAKUMAR	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *1-6,15 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/14/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 7-14, in the reply filed on 06/02/2008 is acknowledged. The traversal is on the ground(s) that the methods of treating diseases share the same special technical feature as the compounds and thus should be rejoined and examined in concert with the compound and pharmaceutical composition claims. This is not found persuasive because it is acknowledged that if unity is present then claims for compounds and methods of using the compounds would be examined together. However as referenced in the previous office action, the common core is known in the prior art (for a different utility) and therefore unity is lacking. The method claims will be rejoined when the compound claims become allowable.

The requirement is still deemed proper and is therefore made FINAL.

Claims 15 and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 06/02/2008.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 9, 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the two natural products, does not reasonably provide enablement for the plethora of possible structures encompassed by the generic formulae and compound 2. For example, it is not seen where in the specification, enabling disclosure is found for allenic structures. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the relevant factual considerations.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: (1) breadth of the claims; (2) nature of the invention; (3) state of the prior art; (4) amount of direction provided by the inventor; (5) the level of predictability in the art; (6) the existence of working examples; (7) quantity of experimentation needed to make or use the invention based on the content of the disclosure; and (8) relative skill in the art.

All of the factors have been considered with regard to the claims, with the most relevant factors discussed below:

The claimed compounds are two polyolefinic, terpenic natural products as well as a wide variety of geometric, stereochemical and structural analogs/derivatives of the said natural products. The claims are also drawn to pharmaceutical use of these compounds. While the specification is enabling for isolating the said two natural products, there is no guidance, direction and working examples present in the specification for making or using any of compounds other than the said two natural products. In addition, the biological data (i.e., potential utility) disclosed for the claimed compounds is limited to in vitro assay data for the two natural products. No chemical schemes for de novo synthesis and/or methods for selective functionalization of the two natural products is found in the specification. For example, any conceivable synthetic sequence to make the 8-10 single bond analogs (Palinurin numbering) as claimed would require undue experimentation because of the need for total synthesis. Alternatively the outcome of any synthetic method to selectively saturate the 8-10 double bond (by controlled hydrogenation, for example) of the natural products would be unpredictable because of the presence of similar multiple double bonds in the natural products. Likewise, the specification does not enable for the selective functionalization of the dione unit of tricantin and thus not enabling for any of the derivatives in claim 11. Further without prior art citation or disclosure in the specification with regards to structural requirements for GSK inhibition, it would be unpredictable which particular embodiment of the compounds of formulae is likely to inhibit GSK. For these reasons,

one skilled in the art would be faced with undue amount of research. The claims are not commensurate in scope with the breadth of enablement in as much as the working example in the application is limited to two compounds compared to the wide breadth of the claims, the unpredictability of the art, the high quantity of experimentation needed to make and use the compounds of the instant claims.

The specification is enabling for compound of claim 8, 10 and 14.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11 and 13 rejected under 35 U.S.C. 102(b) as being anticipated by Alfano et al. Experientia 1979, 35, 1136-1137 (Applicant admitted prior art, see specification page 13, line 10).

Prior Art compound Palinurin is compound of claim 13, and corresponds to compound of claim 11 wherein n = 3, R1 is methyl (alkyl), R is –OH.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

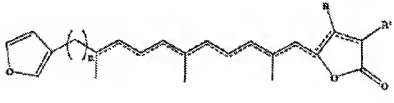
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

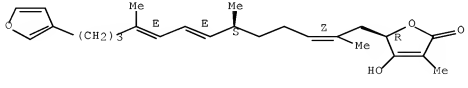
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 9-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu, et al. Journal of Natural Products (2002), 65(9), 1307-1314.

Instant claims are drawn to pharmaceutical compositions of compounds of the following formula



Liu et al. teach pharmaceutical compositions and therapeutic use of compound



as well as furanoterpenoids of similar structure.

Liu et al. do not teach all the wide variety of instantly claimed structures (see

rejection under *35 USC § 112-1)*. Liu et al. also do not teach the biochemical mechanism underlying the pharmaceutical properties of the compounds.

However, since the prior art compound falls within the scope of the instantly claimed formula and is cytotoxic, it would be obvious to one skilled in the art to make minor modifications to the structures of Liu et al. to arrive at compounds within the scope of the Applicant's claims, further because structurally similar compounds are anticipated to possess similar properties.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nizal S. Chandrakumar

/Janet L. Andres/

Supervisory Patent Examiner, Art Unit 1625